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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/441,318	Applicant(s) CONKLIN ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-23 are pending.

2. The drawings as submitted have been approved by the draftsman.

Specification

3. The disclosure is objected to because of the following informalities:

The figure legend to Fig. 3B states that the figure shows the sequence of a 92 kb BAC (T5I7). The figure does not show 92000 bases of sequence, nor does it show any sequence.

The amendment filed 18 June, 2001, requested deletion of the Figure legend to Figure 5 and amended one paragraph referring to Figure 5. These were entered. However, Figure 5 itself is still present in the specification. The Figure must either be cancelled (along with any other mentions of Figure 5 in the text, if they exist) or a new figure legend and the sequences presented in Figure 5 must be submitted in computer readable form.

Appropriate correction is required.

4. The disclosure is objected to because it contains an embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete all the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

5. All instances of sequence in the text (*e.g.*, pg 12, paragraph 1) must be accompanied by the appropriate SEQ ID NOs:. See MPEP § 2422.03 and 37 CFR 1.821(d).

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 23 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claim is drawn to plants comprising a mutant GDP-mannose pyrophosphorylase (GMPase). However, the only utility proposed in the specification for these mutant plants is studying the Vitamin C pathway (pg 17, lines 21-23). This is not a specific utility. Additionally, as the mutant plants described in the specification are killed or injured by treatment that does not affect wild-type plants (pg 8, lines 16-20), it is difficult to imagine a specific use for them.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 23 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a method of increasing the endogenous level of vitamin C in a plant by overexpression by any method of any enzyme crucial to vitamin C biosynthesis,

and plants thereby obtained. Dependent claims limit the method and plants to transformation with a gene encoding GMPase.

The instant specification, however, while discussing expression of an *Arabidopsis* gene encoding GMPase in *vtc1* mutants of *Arabidopsis*, fails to provide guidance for successful overexpression of that gene in wild-type plants.

Overexpression of a gene in plants is unpredictable. Sweetlove et al (1996, Biochem. J. 320:493-498) found no differences in starch content, tuber number, tuber weight, or metabolite content between potatoes transformed with a gene encoding ADP-glucose pyrophosphorylase and potatoes from control plants, even though the activity of the enzyme was four-fold higher in the transformed plants (pg 495, entire pg, and pg 497, right column, paragraph 3). Thiele et al (1999, Plant Physiol. 120:73-81) teach that in potato plants transformed with the *Arabidopsis* phytochrome B gene, the endogenous phytochrome B transcript levels were not significantly affected (pg 75, right column, paragraph 3, and Fig. 1). As the gene encoding GMPase was expressed in wild-type plants, the unpredictability associated with overexpression of genes in plants has not been overcome.

The claims are drawn to methods of increasing vitamin C levels in plants by transformation with any gene encoding GMPase, and plants so transformed. However, the only gene encoding GMPase taught in the instant specification is from Arabidopsis.

Additionally, the instant specification fails to teach any other gene encoding any other enzyme involved in vitamin C biosynthesis. It also fails to teach or suggest any method of overexpressing any enzyme other than by transformation of a gene into a plant; it does not teach,

for example, topical application of an inducer of the promoter of an endogenous gene encoding an enzyme involved in vitamin C biosynthesis.

Claim 23 is drawn to a plant comprising a mutant gene encoding a form of GMPase. The instant specification fails to provide guidance for plants comprising mutant GMPase genes that do not result in the plant being more sensitive to stresses like ozone.

Lastly, the instant specification fails to provide guidance for the sequence of the gene encoding GMPase. Thus, the invention appears to employ novel plasmid encoding GMPase contained in microorganisms. Since the plasmids contained in the microorganisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the plasmids contained in the microorganisms are not so obtainable or available, the requirements of 35 USC 112 may be satisfied by a deposit of the microorganisms. The specification does not disclose a repeatable process to obtain the plasmids contained in the microorganisms and it is not apparent if the plasmids are readily available to the public. Thus, a deposit is required for enablement purpose.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for increasing the endogenous level of vitamin C in a plant by overexpression by any method of any enzyme crucial to vitamin C biosynthesis, including non-*Arabidopsis* GMPase, and plants thereby obtained.

11. Claims 1-23 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to methods for increasing the endogenous level of vitamin C in a plant by overexpression of any gene encoding any enzyme crucial to vitamin C biosynthesis. The specification does not describe which enzymes are crucial for vitamin C biosynthesis, their enzymatic activity, or the sequence of any gene encoding any enzyme involved in vitamin C biosynthesis, including that of any gene encoding GMPase. Furthermore, the specification does not demonstrate the isolation of GMPase genes from plants other than *Arabidopsis*.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed plants and methods, and given the high level of unpredictability in this art, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), where it states:

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA . . . Accordingly, the specification does not provide a written description of the invention . . .

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and . . . conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials . . . . Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

12. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-8, 12-14 and 16-23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Dependent claims are included in the rejections.

Claim 1 is indefinite in its recitation of "protein involved in Vitamin C biosynthesis." The nature of that involvement is not clear.

Claim 16 is indefinite in its recitation of "enzyme crucial to Vitamin C biosynthesis." It is not clear what level of involvement in vitamin C biosynthesis is rated "crucial".

Claims 5 and 12 are indefinite in its recitation of "is capable of overexpressing". The use of this phrase suggests that overexpression is not required for the invention. It is suggested that the phrase be replaced with --that overexpresses--.

Claims 6 and 13 are indefinite in its recitation of "is capable of producing". The use of this phrase suggests that production of increased levels of vitamin C is not required for the invention. It is suggested that the phrase be replaced with --that produces--.

The terms "overexpressing" in claims 5 and 12 and "overexpression" in claim 16 are relative terms that render the claims indefinite. The terms "overexpressing" and "overexpression" are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that the level of expression be compared to that of a nontransformed plant in the claims. Because methods require active, positive steps, it is suggested that "overexpression" in claim 16 also be replaced with --overexpressing--.

The term "increased" in claims 6, 13 and 20 and "increasing" in claim 16 are relative terms that renders the claims indefinite. The terms "increased" and "increasing" are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that the level of vitamin C or antioxidation capacity be compared to that of a nontransformed plant.

Claims 7, 14 and 21 are not written in proper Markush format. The claims should be in the format "selected from the group consisting of A, B, C and D." There should be no colon after "consisting of" and no semicolons between members of the group. See MPEP 2173.05(h) Dependent claims are included in the rejection.

Claim 20 is indefinite in its recitation of "plant ... comprises increased antioxidation capacity". A plant does not comprise increased antioxidation capacity, although increased

antioxidation capacity may be a property of the plant. It is suggested that "comprises" be replaced with --has--.

Claim 23 is indefinite in its recitation of "a form of GDP-mannose pyrophosphorylase." It is unclear what that form is.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

15. Claims 1-2, 5-8, 16-18 and 20-22 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Trulson et al (US Patent 6,143,562, filed April, 1995)

Trulson et al teach tomato, melon, squash and maize plants transformed with a gene encoding phosphomannose isomerase (claims 1-19 and columns 25-30), an enzyme in the vitamin C biosynthetic pathway. The claimed increased stress resistance would have been an inherent property of these plants, as would increased vitamin C levels.

16. Claims 1-3, 5-8, 16, and 18-22 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Bauw et al (WO 98/50558).

Bauw et al teach *Arabidopsis* and tobacco plants transformed with a gene encoding L-galactono-γ-lactone dehydrogenase, an enzyme involved in vitamin C biosynthesis (pg 15-20)

The resulting plants overproduce vitamin C (Table 5), and would be stress resistant (pg 2, lines 16-21).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 3 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trulson et al (*supra*) in view of Schmidt et al (1988, Plant Cell Rep. 7:583-586).

The claims are drawn to *Arabidopsis* plants transformed with a gene encoding a protein involved in vitamin C biosynthesis, and methods of increasing vitamin C levels in *Arabidopsis*.

Trulson et al disclose various dicots transformed with a gene encoding phosphomannose isomerase (claims 1-19 and columns 25-30), an enzyme in the vitamin C biosynthetic pathway; these plants would have increased stress resistance and vitamin C levels. Trulson et al do not disclose *Arabidopsis* plants transformed with that gene.

Schmidt et al teach transformation of Arabidopsis (pg 583-4).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to transform dicots with a gene encoding an enzyme in the vitamin C biosynthetic pathway as taught by Trulson et al, and to modify that to transform *Arabidopsis* with that gene as described in Schmidt et al. One of ordinary skill in the art would have been motivated to do so because the dicot species to be transformed is a design choice.

19. Claims 4, 9-15 and 23 are free of the prior art, given the failure of the prior art to teach a gene encoding GMPase and its expression in plants to increase the levels of vitamin C.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached on Monday through Friday, 8:15 am - 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
July 23, 2001

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638